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Quality Assessment of Drug Therapy

Introduction

Each year since 1996 thirty or more new molecular entities have been approved for clinical use by the U.S. Food and Drug Administration.[1] Dozens more new combinations and dosage forms have also been approved during that same time period. The availability of valuable new agents creates opportunities for improved therapeutic outcomes, but also creates increased opportunities for inappropriate medication use. The clinical pharmacologist is expected to hold generalized expertise in the use of medications which can be applied across the organization in the clinical practice, and in independent and collaborative research activities. Quality assessment and improvement of medication use is an important skill set.

The objective of this chapter will be to review medication use quality issues in an institutional context, and highlight their impact on patient care and clinical research. It will focus on three themes: understanding the medication use system and organizational interests in medication use; understanding the use of drug use monitoring as a tool to improve medication use; and understanding processes to identify and improve medication errors.

Adverse Drug Events

Johnson and Bootman[2] projected that costs of $76 billion a year are attributable to medication misuse. Adverse drug events (ADEs) are instances where patient harm results from the use of medication. This includes both adverse drug reactions and medication errors, many of which are inherently preventable. A 1999 Institute of Medicine report estimated that 98,000 Americans die each year due to medical error.[3] This includes diagnostic mistakes, wrong-site surgery, and other categories of error, including medication errors. Approximately 20 percent of all medical errors are medication related.[4, 5]

A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while medication is in the control of a health care professional, patient or consumer.[6] Not all medication errors reach the patient. These are often referred to as "near misses." They are not usually considered to be ADEs only because no harm was done. Preventable ADEs are a subset of medication errors, which cause harm to a patient.[7,8] Because adverse drug reactions are generally unexpected, they are not presently considered to be a reflection of medication use quality in a classic sense. However, as genetic variances become part of the drug selection consideration it may be possible to predict and avoid many of the reactions that have been unexpected in the past. This offers an opportunity to improve the quality of medication use.

Medication errors are costly and are a diversion from the intended therapeutic objective. Morbidity or mortality are possible outcomes of medication errors. A 1997 study by Bates et al.[9] found that 6.5 ADEs occur for every 100 non-obstetric hospital admissions, and that 28 percent of them were preventable. It also was determined that 42 percent of life-threatening and serious ADEs were preventable. Preventable ADEs were responsible for an increased length of hospital stay of 4.6 days and $5,857 per event. The cost for all ADEs was projected to be a cost of $5.6 million per year just for the institution in which the study was conducted. This study demonstrates that safer medication use, with fewer adverse medication events, is a costeffective target.

The Medication Use Process

Medications are prescribed, distributed, and consumed under the assumption that the therapeutic plan will work as intended to provide the expected outcome. It is clear from previous chapters that there are many biological system issues, which will influence the success of the plan. There are other organizational and societal system issues, which influence the success of the therapeutic plan as profoundly as those biological systems issues. A prescriber writes an order for a medication based upon the best available information, the likely diagnosis and the expected outcome. A pharmacist reviews the requested medication order (prescription), clarifies based upon additional information about the patient or medication (allergies, drug interactions, etc.), prepares the medication for use, counsels the patient about the drug, and gives it to the patient. The patient is responsible for understanding the therapeutic objective, knowing about the drug, creating a daily compliance plan (deciding when to take the drug), watching for good or bad results, and providing feedback to the prescriber or pharmacist regarding planned or unplanned outcomes. This process occurs over a variable period of time, in a system where the key participants of the process seldom speak with each other. Each action creates an opportunity for success or failure. Is there any wonder that the quality and integrity of the system is compromised on a regular basis?

The medication use system in an institutional setting offers even more complexity, with more chances for error. The five subsystems of the medication system in a hospital are selection and procurement of drugs, drug prescribing, preparation and dispensing, drug administration, and monitoring for medication or related effects[10] Evaluation and improvement of medication use quality requires consideration of all of these subsystems. Every time that individual has to read, interpret, decide or act, is yet another opportunity for a mistake to occur. Each of the steps in the medication use process provides an opportunity for correct or incorrect interpretation and implementation of the tactics, which support the therapeutic plan. With this many opportunities for medication misadventures to occur, it is easy to understand why tracking and improving quality is an important aspect of medication use.[11]

Phillips and colleagues[12] found a 236 percent increase in medication error related deaths for hospitalized patients between 1983 and 1993. The same study showed an increase of over 800 percent for outpatient medication error deaths. The reported growth in medication error deaths may be partially attributed to more accurate reporting, but clearly represents a growth in the problem of medication errors from potent drugs. A 1999 study by the American Society of Health-System Pharmacists concluded that five of the top eight concerns of patients regarding hospitalization were related to medication use or medication error.[13] A study by Bates et al.[14] determined that the 56 percent of medication errors in a hospital setting were associated with the ordering process, 6 percent with transcription of written orders, 4 percent with pharmacy dispensing, and 34 percent with administration of medications. Based upon these findings it is easily concluded that there is room for improvement in how medications are used in the inpatient and outpatient setting.

Improving the Quality of Medication Use

There are multiple facets to the quality assessment of medication use. Among them are monitoring of adverse medication events and medication use evaluation programs. In order to improve medication use, Berwick[15] has applied the industrial principles of continuous quality improvement to the health care setting. The critical elements of this approach are collection and use of data with a system focus. Deming[16] has championed the use of the Shewhart Cycle as it relates to continuous quality improvement. The Shewhart Cycle is an approach for implementing systematic change based on data collection and evaluation with each iteration of the cycle. Each time the work cycle is completed there is an obligation to evaluate the impact of any process modification on the result. Modifications which improve the result, are permanently incorporated into the process. Changes with no impact or a negative result will be deleted in the next iteration. Deming's message is that ongoing process and system change, along with measurement of the result, provides the feedback loop to support continuous improvement of the product or service.

Organizational Influences on Medication Use Quality

There are several external organizations and internal elements of the healthcare system that have an interest in optimizing medication use. These include the hospital or health system, the medical staff, the group purchasing organization with which the hospital participates for the contractual purchase of drugs, and external regulatory or accreditation organizations (e.g., Joint Commission on Accreditation of Healthcare Organizations; Health Care Financing Agency, state and local public health agencies, etc.). There is interest in what drugs are used, when they are used, how they are used, the economic impact of drug selection, and outcomes which result in safe and effective use of medications.

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) is the organization which accredits most hospitals, health systems, and home care agencies. A significant element of the overall JCAHO review of patient care involves medication use quality and medication system safety. Accreditation standards for medication-related activities are applied to practice in the organization. Hospitals are expected to present evidence that ordering, dispensing, administration, and monitoring of medications, are overseen by the medical staff. The organization must be able to demonstrate that policies for safe medication use practices are in place. Evidence of ongoing medication use evaluation, adverse medication event investigation, and medication use performance improvement are required to meet the standards. Analogous accrediting organizations are often used for accrediting managed care organizations. State professional boards (medicine, nursing or pharmacy) provide oversight

of specialized domains such as prescribing, dispensing, and administration of medications. Most health care facilities are also regulated by local or state health departments which often have local regulations on medication related issues.

It is the responsibility of the medical staff in a healthcare organization to oversee medication use activities. This includes development of medication use policies, selection of drug products which are appropriate to the needs of the patient population being served, and oversight of the quality of medication use. The Pharmacy and Therapeutics Committee is the normal focal point for medication related activities within the organization. The Pharmacy and Therapeutics Committee develops policies for managing drug use and administration, manages the formulary system, and evaluates the clinical use of drugs.[17]

The exact structure of the Pharmacy and Therapeutics Committee may vary to meet the unique needs and structure of the organization. It routinely reports to the medical staff executive committee or other leadership group within the medical staff organization. The Committee is made up of representatives from the principal medication using services (internal medicine, surgery, pediatrics, etc.) within the organization, plus representatives from the nursing services, pharmacy services, quality improvement program, and hospital administration. The chair of the committee is most frequently a clinician with experience in system-wide activities, and most importantly, an interest in quality use of medications. It is customary for the director of the pharmacy department to serve as the executive secretary for the committee in order to assure a working link between pharmacy department and committee activities.

Pharmacy and Therapeutics Committees usually meet six to twelve times per year. The schedule is dependent upon the traditions of the organization and the amount of work included during the full committee meeting. The agenda should be prepared under the supervision of the committee chair, and distributed well in advance of the meeting to allow all participants to read formulary drug monographs and drug use reports before the meeting. Ongoing elements of many committees are special standing subcommittees or focused task force workgroups. Typical standing subcommittees focus on antimicrobial agents and medication use evaluation. Standing subcommittees are appropriate for providing ongoing special expertise on matters that can be referred back to the full committee for action. The task force workgroup is used to address special limited-scope issues, such as *ad hoc* evaluations of agents within a given therapeutic drug class.

Medication Policy Issues

The Pharmacy and Therapeutics Committee is expected to oversee important policies and procedures associated with the use of medications. Medication policy includes a wide range of issues: from who may prescribe or administer drugs, to what prescribing direction and guidance are appropriate to assure safe and appropriate use of high risk, high volume, high cost or problem prone drugs. Policies are often needed to identify who may prescribe or administer medications, to assure consistent supply or quality of drug products, or to allocate drugs in times of shortage. Responsibility for developing policies to address special circumstances or issues is often delegated to the Pharmacy and Therapeutics Committee by the organization. Examples of this type of policy are special drug class restriction, (e.g. antimicrobial agents) and use of agents for sedation during medical procedures.

Formulary Management

The objective of an active formulary program is to direct medication use to preferred agents, which offer a therapeutic or safety benefit, or an economic advantage for use. A statement of principles of a Sound Drug Formulary System was developed in 2000 by a consortium composed of the United States Pharmacopoeia, the Department of Veterans Affairs, the American Society of Health-System Pharmacists, the Academy of Managed Care Pharmacists, and the National Business Coalition on Health.[18] In this statement, a formulary is defined as "a continuously updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis and or treatment of disease and promotion of health." A specific formulary is intended for use in a defined population. The defined population may be patients in a single hospital, patients seen within a group practice, a managed care patient population (local, regional or national), or even an entire community.

Historically, formulary drug inclusion or exclusion has been used as an administrative hurdle to discourage prescribers from using less desirable drugs. The historical approach to formulary decision making was based upon a simple "on formulary" or "not-on formulary" approach. Formulary drugs were available immediately with no special requirements. Often a formulary drug was selected by the prescriber to avoid a prolonged waiting period for the non-formulary item to be ordered and made available for the patient. This approach was more effective when the array of effective drug choices was somewhat limited, and the principal cost and quality management need was to reduce the number of "me-too" products.

With the advent of many of the newest generation of products, including monoclonal antibodies and cytokine agents, it is not logical to simply limit the formulary availability of these novel agents. Accordingly, the standard for most institutions has been to include these novel drugs with committee approved restrictions and guidelines for use. In the future, genomics and genetic diversity, which can influence toxicity and effectiveness, will play an important role in formulary drug management. The ability to better customize patient-specific drug response will require a more sophisticated approach in selecting the most appropriate drug.

Drug Selection Process

Effective formulary development is based upon the scientific evaluation of drug safety, clinical effectiveness, and cost-impact.[18] That information is used by the committee

to determine the specific value and risk of the drug for the patient population to whom the drug will be administered. The committee evaluates a given drug relative to the disease states typically treated in this population. For instance, the presence or absence of certain tropical diseases may impact on the need to include some antimicrobial agents on the formulary. The evaluation of a drug should include discussion of what doses and duration of therapy might be most appropriate in order to establish guidelines for measuring prescribing quality. In some cases it may be necessary to determine which health care professionals are appropriately trained or qualified to prescribe a particular drug. The committee may elect to restrict the use of a drug to certain specialists (e.g., board trained cardiologists for high-risk antiarrhythmic agents) or the drug may be restricted by the manufacturer or FDA to those prescribers who have received some drug-specific training and been approved by the supplier (e.g., thalidomide).

Economic evaluation of medications is a routine element of formulary development. The development of many effective but expensive drugs, which are likely to cost thousands of dollars for a single short course of therapy or tens of thousands for long-term therapy, has placed financial impact at center stage in product selection. The availability of these high-cost agents, has created a new specialty discipline called pharmacoeconomics. A growing list of academic medical centers have established units which focus research and practice efforts on outcomes measurement of drug therapy. These programs often provide sophisticated evaluations of the economic or quality-of-life elements of drug use.

It is important to understand that drug costs, and their impact, are perceived differently from different perspectives in the health care system. Each component of the health care system (hospital, home care, ambulatory provider) may have a different perspective on the cost of therapy. Hospitals are usually responsible for all drug-related costs (drug, medication administration, laboratory monitoring, etc.) for the finite period of time that a patient is hospitalized. A stand-alone outpatient drug benefit manager might only worry about the drug cost for the non-hospitalized portion of the therapy. The overall health system may be at financial risk for all elements of outpatient and inpatient care. Because each element of the system may be responsible for a different component of the total cost of care, the cost-impact of a given drug product selection may be different for each of them. The "societal perspective" often represents yet another view of drug costs in that it incorporates non-health care costs and the value of lost-days of work and disability. Formulary inclusion is not routinely based upon that level of evaluation but public policy may be influenced by that information.

Most hospitals and health care organizations participate in a purchasing group to leverage volume-driven price advantages. The make up and operations of these groups vary widely but the price agreements and changing landscape of drug pricing add an additional dimension to the drug price factor. A specific drug may be the lowest price option for a given contract period, after which the choice may change. In another variation, a package of prices for bundled items may cause the price for a given item to change depending on the use of yet another item. How this influences formulary decisions is a function of the drug and many other factors.

Formulary Tactics

In addition to drug selection, the Pharmacy and Therapeutics Committee is responsible for considering formulary tactics to support the overall goal of optimal medication use. Several of these tactics have been used successfully to direct drug use toward preferred agents. The most obvious tactic to direct use away from a given agent, is to exclude it from the formulary. The use of non-formulary agents usually triggers some required override, or *post-hoc* review of use by the committee or designated individual. A second tactic involves a global management of medication use by therapeutic class. This tactic can be used to minimize the use of drugs with a less clear profile of therapeutic efficacy or safety. A decision to limit the number of agents from a given drug class can also provide some advantages in price contracting, if formulary inclusion is effective in directing medication use to lower cost agents.

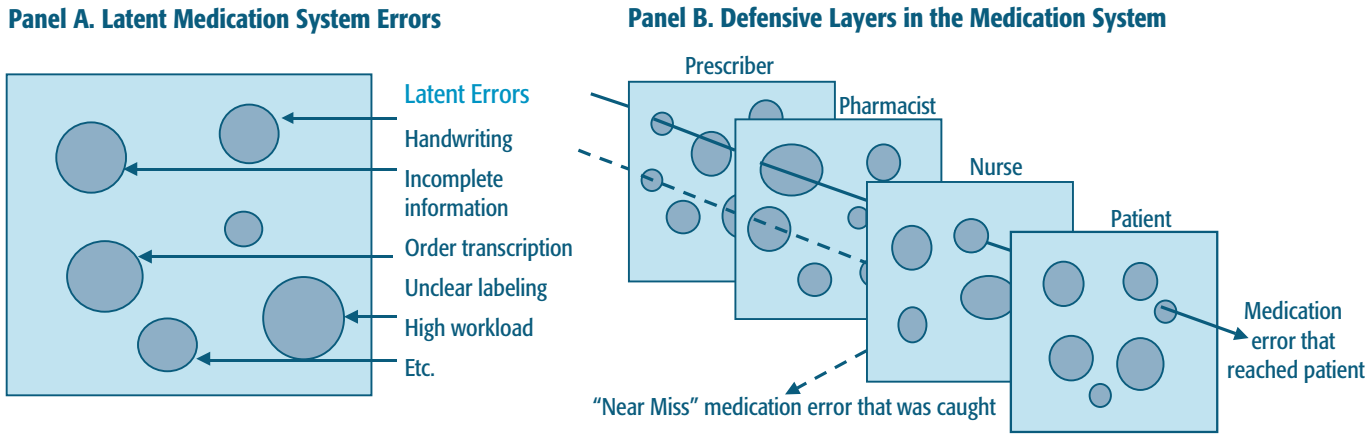
Limiting prescribing rights for some specific drugs to a subset of prescribers who possess special expertise that qualifies them to use these drugs can improve the quality of their use. In many cases, drug restriction is managed by a gatekeeper(s) whose approval is required prior to beginning therapy with the drug (e.g., Infectious Disease approval prior to start of a specified antibiotic). In some cases, direct financial incentives have been used to encourage use of a given drug or group of drugs. These formulary tactics have been used to influence decision making by prescribers, pharmacists, and patients.

Analysis and Prevention of Medication Errors

Reason[19] has described a model for looking at human error that portrays a battle between the sources of error and the system based defenses against them. This model is often referred to as the "Swiss cheese model" as the defenses against error are displayed as thin layers with holes, which are described as latent error in the system. Figure 1 demonstrates the model as applied to medication error. Each opportunity for error is defended by the prescriber, pharmacist, nurse, and patient. When a potential error is identified and corrected (e.g., dose error, route of administration error, etc.) the event becomes a "near miss" rather than an ADE. In those cases in which the holes in the Swiss cheese line up, a preventable medication error occurs. The Swiss cheese model provides an interesting framework for research in this field.

The latent errors in the medication use system have been described in several studies. Major contributors to errors in medication use were found to be: Knowledge gap related to drug therapy (30 percent); Knowledge gap related to patient factors (30 percent); Errors in dose calculations, placement of decimal points, and dosage units (18 percent); Nomenclature failures such as wrong drug

Figure 1. "Swiss Cheese Model"



Latent medication system errors (*Panel A*) and defensive layers against error (*Panel B*) in the medication system.

name, misinterpreted abbreviation, etc. (13 percent).[20] Cohen[21] describes six common causes of medication error based upon his review of events reported to public reporting databases. These causes of errors include failed communication, poor drug distribution practices (including verbal orders), dose miscalculations, drug and device related problems (such as name confusion, labeling or poor design), and lack of patient education on the drugs that are prescribed for their use. Leape et al.[22] identified thirteen proximal causes of medication errors in an academic medical center. They are detailed in Table 1.

Table 1. Proximal Causes of Medication Errors*

Lack of knowledge of the drug	Faulty dose checking
Lack of information about the patient	Infusion pump and parenteral delivery problems
Violation of rules	Inadequate monitoring
Slips and memory lapses	Drug stocking and delivery problems
Transcription errors	Preparation errors
Faulty checking of identification	Lack of standardization
Faulty interaction with other services	

* *Adapted from Leape LL, et al. Systems analysis of adverse drug events. JAMA 1995;274:35-43.*

Medication Error Data

The rate and nature of medication errors has been studied by several authors. Nightingale et al.[23] found a medication error rate of 0.7 percent in a British National Health Service general hospital. Lesar et al.[20] describe the results of a review of 2,103 clinically significant medication errors in an academic medical center. It was determined that 0.4 percent of medication orders were in error: 42 percent of the errors were overdosage, 13 percent were the result of drug allergies which were not accounted for prior to prescribing. This work showed that medication errors result most frequently from failure to alter dose or drug after changes in renal or hepatic status, missed allergies, wrong drug name, wrong dosage form (e.g., IV for IM), use of abbreviations, or incorrect calculation of a drug dose. They concluded that an improved organizational focus on technological risk management and training should reduce errors and patient risk of ADEs.

Given the latent errors associated with some elements of human performance, it seems likely that automation may reduce error. Several studies have demonstrated the value of computer assistance in the medication order entry process. Rules-based physician order systems have been shown to identify and reduce the chances of adverse medication events due to drug duplication, calculation errors and drug-drug interactions.[23, 24-27]

Some therapeutic categories of medications might be predicted to be prone to error due to narrow therapeutic index, complexity of therapy, or other factors. Phillips et al.[12] found that analgesics, central nervous system agents, and non-tranquilizer psychotropic drugs were most frequently associated with deaths due to medication errors. Lesar et al.[20] found antimicrobials, and cardiovascular drugs to be the most error prone therapeutic categories in an academic medical center. The JCAHO has identified a list of drugs and drug practices that are associated with high-risk for significant error, and the Institute for Safe Medication Practices also has identified drugs which should generate a high-alert due to risk for medication errors.[28, 29] Lambert and colleagues[30, 31] have described a series of experiments which test the likelihood of drug name confusion based upon fixed similarity patterns. This theoretical concept is providing the basis for selecting drug names that minimize the chance of sound-alike errors.[32]

Research methods on medication error data are not standardized. Therefore, they are subject to some limitations in generalizability. Because widespread interest in developing scientific approaches for reducing medication error is relatively recent, there are few well-established methods for conducting research in this field. However, funding for research in safe medication use and error reduction is available from several public and private sources including the Agency for Healthcare Research and Quality.

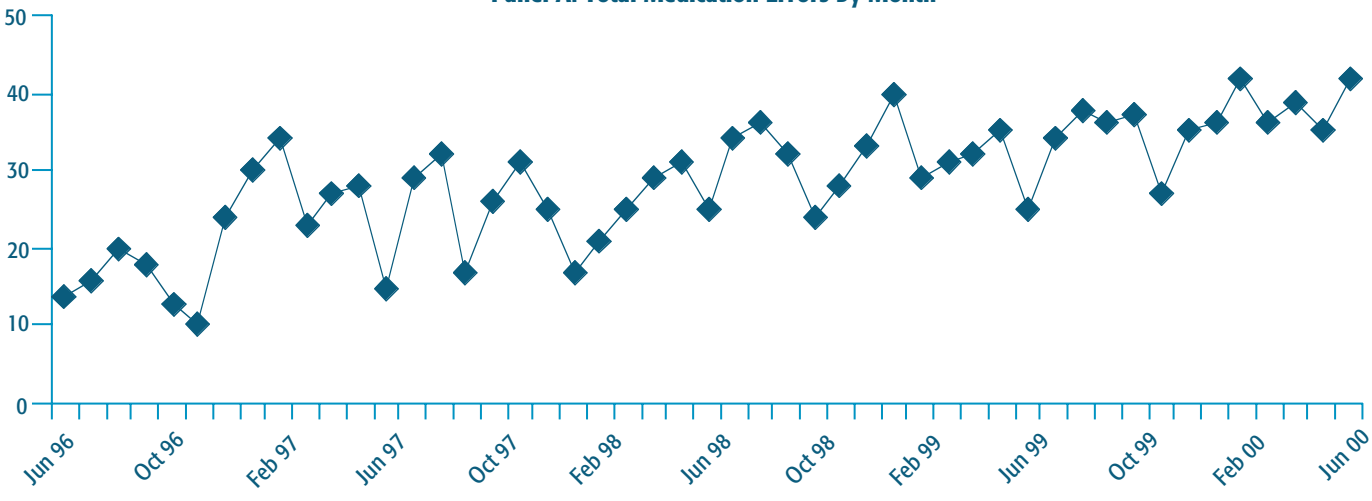
Medication error data collection and analysis for clinical use and quality improvement is also a complex activity. Observational data, *post-hoc* review of medical records, and self-reporting have all have been used with varying degrees of success for research and functional applications. Each offers strengths and weaknesses and the appropriate method for data collection is in large part a function of its intended use and the resources available to collect it.

Most hospitals collect internal medication error data through a voluntary reporting mechanism. This system is used as the backbone of error reporting because it requires minimal resources for data collection, and is supported by organizational risk management programs. Voluntary reporting is presumed to underreport total errors. It is widely believed that most significant errors are reported when they are identified, but many mistakes are never recognized. Many other errors are determined to be insignificant and, therefore, not formally reported. For these reasons, it is difficult to determine in the hospital setting if changes in a given series of numbers represent a real change, or simply a different level of reporting.

Figure 2 illustrates a typical presentation of aggregated or high-level medication error data in an institutional setting. This presentation allows for general trends in total numbers to be plotted and tracked over time. Review of high-level data shows trends and provides a framework for the first level of error analysis. Major

Figure 2. Typical Presentation of Aggregated or High-level Medication Error Data in an Institutional Setting

Panel A. Total Medication Errors by Month



Panel B. Medication Errors by Quarter

	Quarter												
	Jun 97	Sep 97	Dec 97	Mar 98	Jun 98	Sep 98	Dec-98	Mar 99	Jun 99	Sep 99	Dec 99	Mar 00	**Mean**
Wrong Drug	5	3	6	2	10	2	4	5	4	8	2	2	4.4
Wrong Dose	11	17	8	13	6	12	18	17	21	15	22	14	14.5
Duplicate Dose	10	4	3	8	2	16	4	11	9	11	6	17	8.4
Wrong Route	3	2	4	0	2	1	1	5	3	0	3	1	2.1
Wrong Time	15	25	12	33	15	19	27	31	17	26	10	29	21.6
Wrong Fluid	6	7	4	10	3	8	7	5	8	2	3	2	5.4
Wrong Rate	16	20	12	17	21	8	24	8	11	19	23	14	16.1
Wrong Device	2	0	0	1	3	1	4	2	0	1	2	2	1.5
IV Infiltration	0	2	1	0	3	2	0	0	4	0	2	0	1.2
Total	68	80	50	84	65	69	89	84	77	82	73	81	75.2

Typical presentation of medication error data in aggregate form by month (*Panel A*) or catergorized by error type on a quarterly basis (*Panel B*).

changes can be seen which may trigger more intense analysis. However, this high-level data does not provide any detail to the analyst regarding the subcomponents of the composition of the reported errors. As a result, there are pitfalls in drawing conclusions from aggregated high level data that can make these conclusions problematic. For instance, one might presume that administration of medication to the wrong patient is generally more serious than administration of a medication at the wrong time. However, an increase of five "wrong patient" errors and a decrease of five "wrong time" errors for a specific time period will register as a zero change for that period if only aggregated data is used. If fact, it may represent a serious degradation in some element of the medication system which will not be seen through this level of error analysis.

Classification and analysis of medication error data by error type is recommended as a method to spot potentially important changes in system performance. The National Coordinating Council for Medication Error Reporting and Prevention system for classifying medication errors may be used.[12] Commercial systems for cataloging and analyzing medication errors are available. A potentially valuable element of some programs is the ability to share anonymous data with other hospitals for comparison with similar institutions.[33] Regardless of the system used to classify and analyze medication error data, clear and consistent classification must be made to avoid confounding conclusions regarding underlying problems.

Reducing Medication Errors

Collection and use of medication error data at the hospital level is challenging but important. A key organizational principle in quality improvement is to make reporting errors a non-punitive process. This usually increases the number of errors which will be reported, but not the number occurring. Making errors visible is an important step in the process of finding and fixing system related problems.[34] The ongoing monitoring of adverse drug event data (both medication error and adverse drug reactions) is an important responsibility of the Pharmacy and Therapeutics Committee. The Committee is the organization's only point where all of the medication related issues converge. This convergence allows for a full review of the medication use process for system adjustments.

In order to identify opportunities for reduction of medication errors it is important that each error be carefully reviewed by a limited number of individuals to gain intimate knowledge of each reported incident. Collection and classification of error data must be followed by use of a careful epidemiological approach to problem solving at the system level. Narrative data, which may not be seen by looking at the categorical data alone, can be used to provide important details about proximal causes and latent error which may have contributed to the event. Success in this type of error reduction requires the reviewers to read between the lines, to look for common threads between reports, and to link multiple errors which are the result of system weaknesses.

There is still work to be done in understanding errors in the medication use process. However, available information provides suggestions on how to reduce medication errors. Bates[35] ongoing studies of medication errors lead to eight specific error prevention strategies: 1) unit-dose medication dispensing; 2) targeted physician education on optimal medication use; 3) include the clinical pharmacist in decision-making patient activities; 4) computerize medication checking; 5) computerize order entry by the prescriber; 6) standardize processes and equipment; 7) automate medication dispensing systems; and 8) bar-code medications for dispensing and administration. Other authors have reached similar conclusions.

The more complex a patient's drug therapy, the greater the likelihood of adverse medication events. Cullen et al.[36] determined that the rate of preventable and potential adverse drug events was twice as high in intensive care units, compared to non-intensive care units. This is attributed to the higher number of drugs used in the ICU. Lesar et al.[37] reviewed medication prescribing errors over a 9-year period and concluded that the incidence of prescribing error increased as intensity of care increased and new drugs became available. Koechler et al.[38] reported that greater than five current medications, 12 or more doses per day, or medication regimen changes four or more times in a year, were all predictors for drug therapy problems in ambulatory patients. Gray et al.[39] determined that the occurrence of an ADE was positively related to the number of new medications received at hospital discharge. The knowledge that some patients are at higher risk for ADEs suggests possible high-return intervention targets. When selecting improvement opportunities it is wise to look for those areas most likely to yield results.

Examples of system improvements to reduce medication errors have been reported in several projects. Leape et al.[40] reduced medication errors in an intensive care unit by inclusion of a pharmacist on the clinical rounding team. Flynn et al.[41] identified interruptions (telephone calls, conversations, etc.) during critical phases of pharmacist drug preparation activities as significant contributors to errors in medication preparation. Comprehensive efforts to prevent medication errors include the four-pronged medication error analysis program from the Institute for Safe Medication Practices. This four-pronged approach includes evaluation of specific medication errors, evaluation of aggregated error data and near miss data for the hospital, as well as evaluation of error reports from other hospitals.[42] In addition effective medication error prevention includes ongoing monitoring of drug therapy trends, changes in medication use patterns, information from the hospital quality improvement or risk management program, and general hospital programmatic information.

Monitoring institutional trends in medication use can provide clues to possible high risk or error prone therapies. Increased use of drugs with a history of medication errors, such as patient controlled analgesia, should alert organizations to develop safeguards to protect against errors before rather than after they become problems. Cohen and Kilo[43] describe a framework for improvement of use of high-alert drugs, which is based upon reducing or eliminating the possibility of error, making errors visible, and minimizing the consequences of errors. Table 2 presents change concepts for safeguarding when using high-risk drugs.

Medication error prevention opportunities also may present themselves in unusual hospital programmatic information from sources not routinely applied to medication safety. For instance, reports of laboratory related incidents, or hospital information system problems may be indicators that medication related problems can be expected. Thoughtful use of this information may prevent medication related errors attributed to supplemental systems that are critical to safe and appropriate medication use. Reports of staff shortages within an institution (e.g., critical care nursing, nurse anesthetist) can be used to identify potential problem areas prior to medication error reports. Likewise reports of planned construction or information system conversions may be an indicator that routines will be interrupted. This can be used to help provide safe alternatives before errors occur. Use of hospital program information in a prospective way can be used to avoid medication errors.

System improvements may improve the quality of prescribing by standardizing to an expert level. Morris[44] describes the development, testing and use of computerized protocols for management of intravenous fluid and hemodynamic factors in patients with acute respiratory distress syndrome. Evans et al.[45] used a computerized antiinfectives management program to improve the quality of medication use and reduce the costs. In consideration of all that is currently known Leape[46] provides a simple set of recommendations to reduce medical error: Reduce reliance on memory; improve access to information; error proof critical tasks; standardize processes; and instruct health care providers on possible errors in processes. These simple but thoughtful recommendations are an important concept to reduction in medication errors.

Medication Use Evaluation

Medication Use Evaluation (also referred to as drug use evaluation or DUE) is a required component of the medication use quality improvement process. It is a performance improvement method with the goal

Table 2. Safeguarding Against Errors in High-risk Drugs*

Concept	Example
Build in System Redundancies	Independent calculation of pediatric doses by more than one person (e.g., prescriber and pharmacist)
Use Fail-safes	IV pumps with clamps that automatically shut off flow during power outage
Reduce Options	Use of a single concentration of heparin for infusion (e.g., 25,000 units in 250 ml of saline)
Use Forcing Functions	Preprinted order forms for chemotherapy drugs which require patient height and weight information before preparation and dispensing
Externalize or Centralize Error-prone Processes	Prepare IV admixtures in the pharmacy instead of on nursing units
Use Differentialization	Supplemental labels for dosage forms which are not appropriate for intravenous use without dilution
Store Medications Appropriately	Store dopamine and dobutamine in separate locations
Screen New Products	Review new formulary requests for labeling, packaging and medication use issues which may be error prone
Standardize and Simplify Order Communication	Avoid use of verbal orders
Limit Access	Restrict access to the pharmacy during "non-staffed" hours and follow-up on all medications removed from the pharmacy during this time
Use Constraints	Require approval before beginning therapy (e.g., attending signature on chemotherapy orders)
Use Reminders	Place special labels on products when they are dispensed by the pharmacy to remind of special procedures for use (e.g., double check rate calculation of insulin infusions)
Standardize Dosing Procedures	Develop standardized dose and rate charts for products such as vasoactive drugs (e.g., infusion rate expressed as micrograms per kilogram per minute)

* *Adapted from Cohen MR, Kilo CM.* High-Alert Medications: Safeguarding against errors. *In Medication Errors. Washington: American Pharmaceutical Association; 1999 (pages).*

Table 3. Drug Use Review Categories

Review Category	Data Collection Model(s)	Typical Application	Comments
Retrospective	Data is collected for a fixed period which may be archival or accumulation of new patients for a fixed period of time	Data archive search for prescribing patterns of patients on seratonin antagonist antiemetic drugs	Supports large scale epidemiologic approach No active intervention to change medication use patterns occurs due to the post-hoc data collection process
Concurrent	Each new order generates an automatic review of previously approved criteria for use within a specified period of the initiation of therapy	Review of naloxone to investigate possible nosocomial adverse medication event	
	Laboratory or other monitoring criteria are reported for all patients on the drug	Digoxin monitoring based upon daily review of digoxin serum levels[49]	
	Abnormal Laboratory or other monitoring criteria are reported for all patients on the drug on a regular basis	Regular review of serum creatinine for patients on aminoglycosides	
Prospective	Each new order for the drug is evaluated for compliance with previously approved criteria for use. Variance to the criteria require intervention prior to initiation of therapy	Medication use guidelines (ketorolac)[50] Restricted antibiotics	

of optimizing patient outcomes.[47] The first element of drug use tracking is global monitoring of organizational drug use. This can be completed by routine evaluation of totals and changes in drug use within a therapeutic drug category. The American Hospital Formulary Service has created a comprehensive therapeutic classification system that is often used for drug use monitoring, but other commercial medication databases are also available.[48]

Medication use evaluation has historically been categorized with regard to how and when data collection or intervention occurs. Table 3 describes retrospective, concurrent and prospective activities based upon the use and timing of intervention as part of the process which is used for screening and incorporation of data.

Focused Medication Use Evaluation

Focused or targeted medication use evaluation follows a reasonably well-established cycle: identification of a potential problem in the use of a specific drug or therapy, collection and comparison of data, determination of compliance with a pre-established guideline/expectation, and action as needed to improve discrepancies between expected and measured results. Focused medication use projects are typically selected for a specific reason. Table 4 lists reasons to consider drugs for focused evaluation projects.

Concurrent or Prospective Focused Medication Use Review

Concurrent or prospective focused medication use review activities can be used to prevent medication related adverse events and improve the quality of medication use. Information system support has been demonstrated to enhance response to changes in predefined laboratory values. Notice of abnormalities in coagulation, renal function, blood glucose, and electrolytes are all potential indicators of medication use problems in individual patients. When laboratory test results are reported along with specific drugs it is possible to respond to potential

Table 4. Selection of Targets for Focused Medication Use Review*

- Medication is known or suspected to cause adverse reactions or drug interactions
- Medication is used in patients at high risk for adverse reactions
- Medication-use process affects large number of patients or medication is frequently prescribed
- Medication or process is a critical component of care for a specific disease, condition or procedure
- Medication is potentially toxic or causes discomfort at normal doses
- Medication is most effective when used in a specific way
- Medication is under consideration for formulary retention, addition or deletion
- Medication or process is one for which suboptimal use would have a negative effect on patient outcomes or system costs
- Medication is expensive

* *Adapted from American Society of Health-System Pharmacists. ASHP guidelines on medication-use evalutation.* Am J Health Syst Pharm *1996;53:1953-5.*

medication-related problems before serious negative outcomes are seen. Kuperman et al.[51] concluded that incorporation of an automatic alerting system in the laboratory data system resulted in a 38 percent shorter response to appropriate treatment following alert to a critical value.

Strategies for Improving Medication Use

One approach to improving the quality of drug use is the development and implementation of medication use guidelines. This evidential approach to the use of medications is designed to rely on the best available clinical evidence to develop a treatment plan for a specific illness or use of a specific drug or drugs. Simple medication use guidelines can be developed based upon literature and the best judgment of in-house experts. Development of more formal clinical practice guidelines is a complex process, which relies on well defined methods to combine the results of multiple studies to draw statistical conclusions. These sophisticated products are often addressed by professional or governmental organizations.

The use of "counter-detailing" by designated hospital staff to offset the impact of pharmaceutical sales forces has been an effective strategy for improving medication use.[52] The objective of this category of quality improvement program is to educate prescribers regarding the organization's approved and preferred medication use guidelines. This has been implemented by providing literature and prescriber contact from a pharmacist or other staff member, to support the desired medication use objective.

Several approaches have been described for improving medication use through the use of dosing service teams. Demonstrated enhancements in the quality of medication use have been reported for anticoagulants, antimicrobials, anticonvulsants, and other drugs. The common method of these programs is the use of expert oversight (physicians or pharmacists) to manage therapy with the targeted drug. Therapeutic management may rely on algorithms, pharmacokinetic models, or preapproved collaborative plans.[53-63]

Use of standardized medication order forms has been demonstrated to increase quality and effectiveness in medications that are prone to error.[64, 65] Chemotherapy, patient controlled analgesia, and antimicrobial drug therapy are likely candidates for order standardization. Yet another approach to improved medication use is implementation of alert systems for sudden, unexpected actions, such as medication stop orders, or use of antidote type drugs, such as diphenhydramine, hydrocortisone, or naloxone. A computerized application of this method was described by Classen et al.[66]

Summary

The medication use process is a complex system intended to optimize patient outcomes within the organizational constraints. Quality medication use involves selection of the optimal drug, avoidance of adverse medication events and completion of the therapeutic objective. Safe medication practices focus on the avoidance of medication errors. Medication use review and ongoing medication monitoring activities focus on optimizing medication selection and use. These two approaches are important means of assessing and optimizing the quality of medication use.

References available upon request.

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